80354

From: Chan, Christina
Sent: Monday, November 18, 2002 8:20 AM
To: Nguyen, Quang (AU1632); STIC-Biotech/ChemLib
Subject: RE: Rush sequence search request for 09/829004

Please rush. Thanks Chris

Chris Chan
TC 1600 New Hire Training Coordinator and SPE 1644
308-3973
CM-1, 9B19

-----Original Message-----
From: Nguyen, Quang (AU1632)
Sent: Sunday, November 17, 2002 12:00 PM
To: Chan, Christina
Subject: Rush sequence search request for 09/829004

I would like to request for a RUSH sequence search for the above amended case because I would like to get it done this bi-week.

Please search:

A nucleic acid molecule encoding SEQ ID NO: 7, 8 and 9, against commercial, issued and pending US patent application databases.

I am in AU1636, my mailbox is in CM1-11E12.

THANK YOU.

Point of Contact:
Toby Port
Technical Info. Specialist
CM1 6A04
703-308-3534

	TYPE OF SEARCH:	VENDOR/COST (where applic.)
Searcher:_____	NA Sequences:_____	STN:_____
Phone:_____	AA Sequences:_____	DIALOG:_____
Location:_____	Structures:_____	Questel/Orbit:_____
Date Picked Up: 11/18	Bibliographic:_____	DRLink:_____
Date Completed: 11/19	Litigation:_____	Lexis/Nexis:_____
Searcher Prep/Review:_____	Full text:_____	Sequence Sys.:_____
Clerical:_____	Patent Family:_____	WWW/Internet:_____
Online time:_____	Other:_____	Other (specify):_____

clinical trial of cytotox[redacted]T lymphocyte (*CTL*) precursor[redacted]iented peptide vaccine therapy is ongoing to evaluate its safety and biologic effects in 9 patients with HRPC at our institute. End points include toxicity, serum prostate-specific antigen (*PSA*) rise, and immunologic effects as measured by ELISA for *CTL* activity and anti-peptide IgG antibody induction. Toxicity was minimal, and dose-limiting toxicity was not observed. *CTL* activity was induced after the cancer vaccine therapy in 5 patients (56%). Of the 9 patients, 1 patient had a partial response and a greater than 50% reduction in *PSA*. In 1 patient achieving stable disease, bone metastasis recognized on a bone scan before treatment disappeared after the cancer vaccine therapy. Six patients showed progressive...

...cancer. Tolerance of the cancer vaccine therapy and the immunologic response were generally good. The clinical responses of this trial have been limited but promising. *Immunotherapy* using *CTL* precursor-oriented peptide vaccine may become an effective modality of *prostate* *cancer* treatment in the future.
?ds

Set	Items	Description
S1	14880	(PSA OR PSMA OR PAP) (S) (PROSTATE (W) CANCER)
S2	197	S1 (S) (IMMUNOTHERAPY OR (IMMUNOGENIC (W) PEPTIDE))
S3	22	S2 AND (PLASMID OR VECTOR)
S4	11	RD (unique items)
S5	38	S2 AND (MHC OR CTL)
S6	20	S5 AND (EPITOPE)
S7	9	RD (unique items)
S8	8	S7 NOT S4
S9	19	RD S5 (unique items)
S10	11	S9 NOT S7

?logoff
03dec02 11:11:39 User259876 Session D441.2
$1.93 0.604 DialUnits File155
$2.94 14 Type(s) in Format 3
$2.94 14 Types
$4.87 Estimated cost File155
$1.17 0.396 DialUnits File159
$1.30 5 Type(s) in Format 3
$1.30 5 Types
$2.47 Estimated cost File159
$2.83 0.506 DialUnits File5
$15.75 9 Type(s) in Format 3
$15.75 9 Types
$18.58 Estimated cost File5
$5.69 0.632 DialUnits File73
$5.00 2 Type(s) in Format 3
$5.00 2 Types
$10.69 Estimated cost File73
OneSearch, 4 files, 2.138 DialUnits FileOS
$2.16 TELNET
$38.77 Estimated cost this search
$39.16 Estimated total session cost 2.239 DialUnits

Status: Signed Off. (10 minutes)

Status: Path 1 of [Dialog Information Services via Modem]

Status: Initializing TCP/IP using (UseTelnetProto 1 ServiceID pto-dialog)
Trying 31060000009999...Open

DIALOG INFORMATION SERVICES
PLEASE LOGON:
 ******** HHHHHHHH SSSSSSSS?
Status: Signing onto Dialog
 ****
ENTER PASSWORD:
 ******** HHHHHHHH SSSSSSSS? ********
Welcome to DIALOG
Status: Connected

Dialog level 02.11.01D

Last logoff: 29nov02 12:52:33
Logon file001 03dec02 11:01:54
           *** ANNOUNCEMENT ***
                    ***
--File 515 D&B Dun's Electronic Business Directory is now online
completely updated and redesigned. For details, see HELP NEWS 515.
                    ***
--File 990 - NewsRoom now contains May 2002 to present records.
File 993 - NewsRoom archive contains 2002 records from January 2002-
April 2002. To search all 2002 records, BEGIN 990,993 or B NEWS2002.
                    ***
--Alerts have been enhanced to allow a single Alert profile to be
stored and run against multiple files. Duplicate removal is available
across files and for up to 12 months. The Alert may be run according
to the file's update frequency or according to a custom
calendar-based schedule. There are no additional prices for these
enhanced features. See HELP ALERT for more information.
                    ***
--U.S. Patents Fulltext (File 654) has been redesigned with
new search and display features. See HELP NEWS 654 for
information.
                    ***
--Connect Time joins DialUnits as pricing options on Dialog.
See HELP CONNECT for information.
                    ***
--CLAIMS/US Patents (Files 340,341, 942) have been enhanced
with both application and grant publication level in a
single record. See HELP NEWS 340 for information.
                    ***
--SourceOne patents are now delivered to your email inbox
as PDF replacing TIFF delivery. See HELP SOURCE1 for more
information.
                    ***
--Important news for public and academic
libraries. See HELP LIBRARY for more information.
                    ***
--Important Notice to Freelance Authors--
See HELP FREELANCE for more information
                    ***
For information about the access to file 43 please see Help News43.
***
NEW FILES RELEASED
***Dialog NewsRoom - Current 3-4 months (File 990)
***Dialog NewsRoom - 2002 Archive (File 993)
***Dialog NewsRoom - 2001 Archive (File 994)
***Dialog NewsRoom - 2000 Archive (File 995)
***TRADEMARKSCAN-Finland (File 679)

***TRADEMARKSCAN-Norway (File 678)
***TRADEMARKSCAN-Sweden (File 675)
***

UPDATING RESUMED
***Delphes European Business (File 481)
***

RELOADED
***D&B Dun's Electronic Business Directory (File 515)
***U.S. Patents Fulltext 1976-current (File 654)
***Population Demographics (File 581)
***Kompass Western Europe (File 590)
***D&B - Dun's Market Identifiers (File 516)

REMOVED
CSA Files:
***Abstracts in New Technologies and Engineering (File 238)
***Aerospace Database (File 108)
***Aluminium Industry Abstracts (File 33)
***Applied Social Sciences Index and Abstracts (File 232)
***Aquatic Sciences and Fisheries Abstracts (File 44)
***ARTbibliographies Modern (File 56)
***Ceramic Abstracts (File 335)
***Conference Papers Index (File 77)
***Engineered Materials Abstracts (File 293)
***ISMEC: Mechanical Engineering Abstracts (File 14)
***Life Sciences Collection (File 76)
***Linguistics and Language Behavior Abstracts (File 36)
***LISA (Library & Information Science Abstracts) (File 61)
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***METADEX: Metals Science (File 32)
***Oceanic Abstracts (File 28)
***Pollution Abstracts (File 41)
***Sociological Abstracts (File 37)
***Water Resources Abstracts (File 117)
Other files:
***Chicago Tribune (File 632)
***Fort Lauderdale Sun Sentinel (File 497)
***The Orlando Sentinel (File 705)
***Newport News Daily Press (File 747)
***U.S. Patents Fulltext 1980-1989 (File 653)
***Washington Post (File 146)
***Books in Print (File 470)
***Court Filings (File 793)
***Publishers, Distributors & Wholesalers of the U.S. (File 450)
***State Tax Today (File 791)
***Tax Notes Today (File 790)
***Worldwide Tax Daily (File 792)

New document supplier
IMED has been changed to INFOTRIE (see HELP OINFOTRI)

>>> Enter BEGIN HOMEBASE for Dialog Announcements <<<
>>> of new databases, price changes, etc. <<<
****
KWIC is set to 50.
HILIGHT set on as '*'
* ** **

File 1:ERIC 1966-2002/Nov 11
(c) format only 2002 The Dialog Corporation

Set	Items	Description

Cost is in DialUnits
?b 155, 159, 5, 73

```
      03dec02 11:02:08 U[redacted]259876 Session D441.1
           $0.35    0.101 DialUnits File1
     $0.35  Estimated cost File1
     $0.04  TELNET
     $0.39  Estimated cost this search
     $0.39  Estimated total session cost   0.101 DialUnits


SYSTEM:OS  - DIALOG OneSearch
  File 155:MEDLINE(R)  1966-2002/Nov W3
*File 155: For updating information please see Help News155. Alert
feature enhanced with customized scheduling. See HELP ALERT.
  File 159:Cancerlit  1975-2002/Oct
         (c) format only 2002 Dialog Corporation
  File   5:Biosis Previews(R)  1969-2002/Nov W4
         (c) 2002 BIOSIS
*File   5: Alert feature enhanced for multiple files, duplicates
removal, customized scheduling. See HELP ALERT.
  File  73:EMBASE  1974-2002/Nov W4
         (c) 2002 Elsevier Science B.V.
*File  73: Alert feature enhanced for multiple files, duplicates
removal, customized scheduling. See HELP ALERT.

      Set  Items  Description
      ---  -----  -----------
?s (PSA or PSMA or PAP) (s) (prostate (w) cancer)
           29828  PSA
             611  PSMA
           25870  PAP
          200509  PROSTATE
         2190210  CANCER
      S1   14880  (PSA OR PSMA OR PAP) (S) (PROSTATE (W) CANCER)
?s s1 (s) (immunotherapy or (immunogenic (w) peptide))
           14880  S1
          112297  IMMUNOTHERAPY
           36660  IMMUNOGENIC
          670255  PEPTIDE
             584  IMMUNOGENIC(W)PEPTIDE
      S2     197  S1 (S) (IMMUNOTHERAPY OR (IMMUNOGENIC (W) PEPTIDE))
?s s2 and (plasmid or vector)
             197  S2
          180538  PLASMID
          210268  VECTOR
      S3      22  S2 AND (PLASMID OR VECTOR)
?rd
...completed examining records
      S4      11  RD (unique items)
?t s4/3,k/all

 4/3,K/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13518448   22117336   PMID: 12121733
  Induction of antibodies against prostate-specific membrane antigen (PSMA)
by vaccination with a PSMA DNA *vector*.
  Kuratsukuri  Katsuyuki; Wang Ching Y; Sone Tomomichi; Nishisaka Nobuyasu;
Jones Richard E; Haas Gabriel P
  Department  of  Urology,  VA Medical Center, SUNY Upstate Medical
University, Syracuse, NY13210, USA.
  European  urology (Netherlands)  Jul  2002,  42  (1)  p67-73, ISSN
0302-2838   Journal Code: 7512719
  Contract/Grant No.: 1S10RR12917-01A1; RR; NCRR
  Document type: Journal Article
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: In Process
```

Induction of antibodies against prostate-specific membrane antigen (PSMA) by vaccination with a PSMA DNA *vector*.

INTRODUCTION AND OBJECTIVES: Prostate-specific membrane antigen (*PSMA*) is a 750 amino acid surface protein expressed primarily in prostate epithelium, and is upregulated 10-fold in *prostate* *cancer*. It is therefore an attractive target for *immunotherapy*. However, most reported antibodies to *PSMA* apparently recognize epitopes in the residue 43-570 region of the extracellular domain, and upon binding are rapidly removed from the cell surface by internalization. This would potentially limit their ability to mediate Fc-dependent cytoxicity. In this study, we constructed a DNA expression *vector*, pV/TM-PSMc, in which this region was deleted from full-length *PSMA* cDNA. Mice were vaccinated with pV/TM-PSMc DNA to determine whether humoral responses directed against *PSMA*-positive human *prostate* *cancer* cells could be induced by this C-terminal region. METHODS: Polymerase chain reaction (PCR)-based techniques were used to delete codons 50-570 from the coding region of human *PSMA* cDNA, thereby joining the C-terminal end (PSMc) to the N-terminal cytoplasmic/transmembrane domain (TM). This truncated product, TM-PSMc, was cloned into the *vector* pNGVL3 (pV). The resulting *vector*, pV/TM-PSMc, was confirmed by DNA sequencing, and by expression studies using reverse transcriptase (RT)-PCR for transcripts and immunohistochemical (IHC) staining with the *PSMA* monoclonal antibody (mAb) 7E11.C5. BALB/c mice were injected in the tibialis anterior muscle four times, at biweekly intervals, with 100 microg *vector* DNA per injection. One week after the last injection, blood was drawn for serum preparation. The serum was assayed for antibodies against *PSMA* by IHC staining of LNCaP, a *PSMA* -positive human *prostate* *cancer* line. Expression in vaccinated muscle cells was determined by RT-PCR assay for TM-PSMc transcripts. RESULTS: NIH3T3 cells transfected with pV/TM-PSMc stained positively by IHC reaction with mAb 7E11.C5. 48h after one intramuscular (i.m.) injection of mice with 100 microg pV/TM-PSMc *vector* DNA, TM-PSMc transcripts were detectable in muscle RNA by RT-PCR analysis. Anti-serum from pV/TM-PSMc-DNA vaccinated mice, at a dilution of 1:20, intensely IHC-stained both live and fixed LNCaP cells. CONCLUSIONS: These results demonstrate that anti-*PSMA* humoral responses were induced by i.m. injection of mice with pV/TM-PSMc DNA. Antibodies in the anti-serum were directed against extracellular epitopes of native *PSMA* expressed by human *prostate* *cancer* cells. Vaccination with DNA expression vectors such as pV/TM-PSMc may provide an immunotherapeutic approach for the treatment of *prostate* *cancer*.

4/3,K/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13027781 21659355 PMID: 11801539

Identification and characterization of a human agonist cytotoxic T-lymphocyte epitope of human prostate-specific antigen.

Terasawa Hiroshi; Tsang Kwong-Yok; Gulley James; Arlen Philip; Schlom Jeffrey

Laboratory of Tumor Immunology and Biology, Center for Cancer Research, National Cancer Institute, NIH, Bethesda, Maryland 20892, USA.

Clinical cancer research : an official journal of the American Association for Cancer Research (United States) Jan 2002, 8 (1) p41-53 , ISSN 1078-0432 Journal Code: 9502500

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

One potential target of vaccine therapy for human *prostate* *cancer* is the prostate-specific antigen (*PSA*). One strategy to enhance the immunogenicity of a self-antigen such as *PSA* is to develop agonist epitopes that are potentially more immunogenic. The studies described here report the design and analysis of an agonist epitope designated *PSA*-3A ("A" for agonist) of the *PSA*-3 CTL epitope. Studies demonstrate that when

compared with the native *PSA*-3 epitope, the *PSA*-3A agonist demonstrates enhanced binding to the MHC class I A2 allele as well as enhanced stability of the peptide-MHC complex. T-cell lines generated with either the *PSA*-3 or the *PSA* -3A peptide showed higher levels of lysis of targets pulsed with the *PSA*-3A peptide than those targets pulsed with the *PSA*-3 peptide; this was observed when both the concentration of peptide and the ratio of effector to target cells were titrated. T cells stimulated with dendritic cells (DCs) pulsed with *PSA*-3A peptide produced higher levels of IFN-gamma than did DCs pulsed with *PSA*-3 peptide; however, no increase in apoptosis was seen in T cells stimulated with the *PSA*-3A agonist compared with those stimulated with *PSA*-3. Human T-cell lines generated with the *PSA*-3A agonist had the ability to lyse human prostate carcinoma cells expressing native *PSA* in an MHC-restricted manner. Recombinant vaccinia viruses were also constructed that contained the entire *PSA* transgene with and without the single amino acid change that constitutes the *PSA*-3A epitope; DCs infected with the recombinant *vector* containing the agonist amino acid change within the entire *PSA* gene (designated rV-*PSA*-3A) were more effective than DCs infected with the rV-*PSA* *vector* in enhancing IFN-gamma production by T cells. Finally, the *PSA*-3A agonist was shown to induce higher levels of T-cell activation, compared with the *PSA* -3 peptide, in an in vivo model using HLA-A2.1/K(b) transgenic mice. These studies thus demonstrate the potential use of the *PSA*-3A agonist epitope in both peptide- and *vector*-mediated *immunotherapy* protocols for *prostate* *cancer*.

4/3,K/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12519539 21311497 PMID: 11418309

In vivo transfection and/or cross-priming of dendritic cells following DNA and adenoviral immunizations for immunotherapy of cancer--changes in peripheral mononuclear subsets and intracellular IL-4 and IFN-gamma lymphokine profile.

Mincheff M; Altankova I; Zoubak S; Tchakarov S; Botev C; Petrov S; Krusteva E; Kurteva G; Kurtev P; Dimitrov V; Ilieva M; Georgiev G; Lissitchkov T; Chernozemski I; Meryman H T

Biomedical Research Institute, 12111 Parklawn Drive, Rockville, MD 20852, USA. mcamsm@gwu.edu

Critical reviews in oncology/hematology (Ireland) Jul-Aug 2001, 39 (1-2) p125-32, ISSN 1040-8428 Journal Code: 8916049

Document type: Clinical Trial; Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

... express membrane bound molecules (CD80, CD86). Furthermore, patient dendritic cells can be loaded with tumor-associated antigens or peptides derived from them and used for *immunotherapy*. Genetic modification of dendritic cells can also lead to presentation of tumor-associated antigens. Transfection of dendritic cells with DNA encoding for such antigens can...

... tumor specific DNA. Naked DNA immunization offers several potential advantages over viral mediated transduction. Among these are the inexpensive production and the inherent safety of *plasmid* vectors, as well as the lack of immune responses against the carrier. The use of viral vectors enhances the immunogenicity of the vaccine due to...

... studies have suggested that the best strategy for achieving an intense immune response may be priming with naked DNA followed by boosting with a viral *vector* . We have successfully completed a phase I and phase II clinical trials on *immunotherapy* of *prostate* *cancer* using naked DNA and adenoviral immunizations against the prostate-specific membrane antigen (*PSMA*) and phase I clinical trial on colorectal cancer using naked DNA immunization against the carcinoembryonic antigen (CEA). The vaccination was tolerated well and no side...

4/3,K/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10819147 20355043 PMID: 10895014
Naked DNA and adenoviral immunizations for immunotherapy of prostate cancer: a phase I/II clinical trial.
Mincheff M; Tchakarov S; Zoubak S; Loukinov D; Botev C; Altankova I; Georgiev G; Petrov S; Meryman H T
American Foundation for Biological Research, Rockville, MD 20852, USA. mincheffm@netscape.net
European urology (SWITZERLAND) Aug 2000, 38 (2) p208-17, ISSN 0302-2838 Journal Code: 7512719
Document type: Clinical Trial; Clinical Trial, Phase I; Clinical Trial, Phase II; Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

... vectors that carry the tumor-specific DNA. Using the prostate-specific membrane antigen (PSMA) as a target molecule, we have initiated a clinical trial for *immunotherapy* of *prostate* *cancer*. The primary objective of the study was to determine the safety of the *PSMA* vaccine after repeated intradermal injections. METHODS: We have included the extracellular human *PSMA* DNA as well as the human CD86 DNA into separate expression vectors (*PSMA* and CD86 plasmids), and into a combined *PSMA* /CD86 *plasmid*. In addition, the expression cassette from the *PSMA* *plasmid* was inserted into a replication deficient adenoviral expression *vector*. Twenty-six patients with *prostate* *cancer* were entered into a phase I/II toxicity-dose escalation study, which was initiated in spring 1998. Immunizations were performed intradermally at weekly intervals. Doses ...

... used. RESULTS AND CONCLUSION: No immediate or long-term side effects following immunizations have been recorded. All patients who received initial inoculation with the viral *vector* followed by *PSMA* *plasmid* boosts showed signs of immunization as evidenced by the development of a delayed-type hypersensitivity reaction after the *PSMA* *plasmid* injection. In contrast, of the patients who received a *PSMA* *plasmid* and CD86 *plasmid*, only 50% showed signs of successful immunization. Of the patients who received *PSMA* *plasmid* and soluble GM-CSF, 67% were immunized. However, all patients who received the *PSMA*/CD86 *plasmid* and sGM-CSF became immunized. The patients who did not immunize during the first round were later successfully immunized after a boost with the viral *vector* . The heterogeneity of the medical status and the presence in many patients of concomitant hormone therapy does not permit unequivocal interpretation of the data with respect to the effectiveness of the therapy. However, several responders, as evidenced by a change in the local disease, distant metastases, and *PSA* levels, can be identified. A phase II clinical study to evaluate the effectiveness of the therapy is currently underway.

4/3,K/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08518345 95277727 PMID: 7538903
The presence of prostate-specific antigen-related genes in primates and the expression of recombinant human prostate-specific antigen in a transfected murine cell line.
Karr J F; Kantor J A; Hand P H; Eggensperger D L; Schlom J
Laboratory of Tumor Immunology and Biology, National Cancer Institute, NIH, Bethesda, Maryland 20892, USA.
Cancer research (UNITED STATES) Jun 1 1995, 55 (11) p2455-62, ISSN 0008-5472 Journal Code: 2984705R

Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Human prostate-specific antigen (*PSA*) has been shown as an aid in the early detection of *prostate* *cancer* (W. J. Catalona et al., J. Am. Med. Assoc., 270: 948-954, 1993) and was approved in 1994 by the Food and Drug Administration for early detection of *prostate* *cancer*. Immunotherapies directed against *PSA* have been suggested in patients with metastatic *prostate* *cancer* . One of the essential questions is to define which nonhuman species express *PSA* for experimental studies. Using Southern blot analyses, genes related to human *PSA* have been detected in several nonhuman primate species, including chimpanzee, orangutan, gorilla, macaque, and rhesus monkey, but not in other mammalian species, including rabbit, cow, pig, dog, rat, or mouse. Immunohistochemical staining with anti-human *PSA* antisera detected strong staining in both human and monkey prostatic epithelial cells with no reactivity to rat prostate cells. Because the *PSA* gene is not present in the murine genome, a matched set of murine cell lines has been developed that may be useful to study the biochemical functions of *PSA* and as an experimental target for *PSA*-directed *immunotherapy* . To establish such cell lines, a C57BL/6 murine colon adenocarcinoma cell line, MC-38, was transfected with a retroviral *vector* containing cDNA encoding the human *PSA* gene. Genetic analysis of a *PSA*-secreting clone, *PSA*/MC-38, demonstrated that the *PSA* gene had been stably integrated into the MC-38 genome. The *PSA*/MC-38 cell line was found to secrete *PSA* into tissue culture medium, producing a protein of approximately M(r) 30,000. In vivo, *PSA*/MC-38 grew as a s.c. tumor in male and female mice. *PSA*/MC-38 tumors grew more rapidly in athymic mice than in syngeneic C57BL/6 mice, and in both mouse strains, the *PSA*/MC-38 tumors grew more slowly than control *vector*-transduced tumors. *PSA* was detected in the serum and tumors of *PSA*/MC-38 tumor-bearing mice. It is proposed that *PSA*/MC-38 cells may be used as a murine tumor model to test potential therapeutic vaccines and other experimental therapies directed against *PSA*.

4/3,K/6 (Item 1 from file: 159)
DIALOG(R)File 159:Cancerlit

02507306 PMID: 98701203
BIOACTIVITY OF AUTOLOGOUS IRRADIATED PROSTATE CANCER VACCINES GENERATED BY EX VIVO GM-CSF GENE TRANSFER (Meeting abstract).
Simons; Carducci; Weber; Marzo A D; Baccala; Cohen; Clift; Mikhak; Piantadosi; Partin; Carter; Levitsky; Marshall; Mulligan; Nelson
Johns Hopkins University, Baltimore, MD, Cell Genesys Corporation, (L.C., S.M.C.), Foster City, CA.
Proc Annu Meet Am Soc Clin Oncol 1998, 17,
Document Type: MEETING ABSTRACTS
Languages: ENGLISH
Main Citation Owner: NOTNLM
Record type: Completed

...stimulating factor (GM-CSF) gene-transduced, irradiated tumor vaccines induce potent T-cell-mediated antitumor immune responses in poorly immunogeneic preclinical animal cancer models including *prostate* *cancer* . A Phase I trial evaluated this gene therapy strategy in patients with metastatic *prostate* *cancer* (PCA T2c-3/N+M0) found at radical prostatectomy. Eight patients were treated [times]3--6 cycles as outpatients with irradiated, autologous PCA vaccine cells after ex vivo human GM-CSF gene transfer using the MFG retrovirus *vector*. A limitation of this treatment approach was ex vivo vaccine cell expansion (3/11 cases); ex vivo GM-CSF gene transfer was 100% successful (8...

... dendritic cells, macrophages, and degranulating eosinophils surrounding

vaccine cells. Histologically confirmed DTH reactivity to untransduced, autologous PCA target cells was also observed. The median serum *PSA* before surgery was 28.85 (range of 6.7--75) and the median *PSA* level at first vaccination was 0.65 (range of 0.1--30.4). By ultrasensitive serum *PSA* , 6/8 patients progressed after surgery and vaccination. The range of follow up was 51--83 weeks. This study represents a clear demonstration of immunity to cells derived from prostate cancers in humans and should provide a rationale for *immunotherapy* of *prostate* *cancer* using GM-CSF transduced vaccines in controlled efficacy trials. Supported by CaPCURE Clinical Trials Consortium, NIH S.P.O.R.E. In *Prostate* *Cancer*, CA 58230. (C) American Society of Clinical Oncology 1998.

4/3,K/7 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13591713 BIOSIS NO.: 200200220534
Retrovirally-transduced dendritic cell vaccines boost immunity to prostate antigen-expressing murine tumors.
AUTHOR: Medin Jeffrey A(a); Liang Sheng-Ben(a); Qin Gangjian(a); Hou Jeannie; Fowler Daniel
AUTHOR ADDRESS: (a)Division of Experimental Therapeutics, Ontario Cancer Institute, Toronto, ON**Canada
JOURNAL: Blood 98 (11 Part 1):p697a-698a November 16, 2001
MEDIUM: print
CONFERENCE/MEETING: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Our goal is to develop *immunotherapy* for refractory *prostate* *cancer*. Gene transfer into dendritic cells offers the possibility of long-term, stable expression and presentation of tumor antigens. Towards this goal we have designed recombinant oncoretroviral vectors that transfer human prostate specific antigen (*PSA*; in a bicistronic *vector* format with huCD25, a cell surface marker) and human prostate specific membrane antigen (*PSMA*). We have isolated high titer ecotropic and amphotropic *vector* producer clones and demonstrated secretion of *PSA* and cell surface expression of huCD25 or *PSMA* in recipient cells. Next we optimized transduction and differentiation of murine bone marrow-derived dendritic cells (DCs). We found transduced DCs retain expression of co-stimulatory and adhesion molecules, and potently stimulate allogeneic MLR. Furthermore, we observed that DC/*PSA* or DC/*PSMA* can be utilized for primary in vitro sensitization to generate syngeneic murine T lymphocytes with enhanced cytokine production in response to prostate antigen-expressing tumor cells. Most importantly, we have also demonstrated that DC/*PSA*- or DC/*PSMA*, when administered alone as an in vivo vaccine, can protect against tumor challenge from syngeneic MOPC tumors engineered to express prostate antigens. In this model...

...or s.q. (4X105 DC per recipient; in two doses separated by 4 weeks). Transduced DC presented tumor antigen in vivo, as recipients of DC/*PSA* had statistically significant increases in serum anti-*PSA* levels (as measured by ELISA) that was augmented by the second DC vaccination. We also engineered MOPC 315 BALB/c plasmacytoma cells to express huPSA, *PSA*/huCD25, *PSMA*, and control/huCD25. After 18 weeks we challenged vaccinated animals with engineered MOPC cells and measured tumor sizes over the next 20 days. Most significantly, we found that recipients of the DC/*PSA*, when challenged with *PSA*-expressing MOPC tumor cells were completely protected from tumor challenge (5/5 recipients). This marked immunity appeared to be antigen-specific, as recipients of mock-transduced DC or DC/*PSMA* did not have increased protection from challenge with the *PSA*-expressing MOPC tumor cells. These observations

demonstrate that our approach of transducing complete tumor antigens into DC represents a promising strategy for the adoptive *immunotherapy* of cancer, including *prostate* *cancer*.

4/3,K/8 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13348916 BIOSIS NO.: 200100556065
Immunization with type 5 adenovirus recombinant for a tumor antigen in combination with recombinant canarypox virus (ALVAC) cytokine gene delivery induces destruction of established prostate tumors.
AUTHOR: Elzey Bennett D; Siemens D Robert; Ratliff Timothy L; Lubaroff David M(a)
AUTHOR ADDRESS: (a)Department of Urology, The University of Iowa, 200 Hawkins Drive, 3 RCP, Iowa City, IA, 52242-1089: david-lubaroff@uiowa.edu **USA
JOURNAL: International Journal of Cancer 94 (6):p842-849 15 December, 2001
MEDIUM: print
ISSN: 0020-7136
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

...ABSTRACT: and has a highly restricted tissue distribution. Prostatic malignancies in 95% of patients continue to express PSA, making this antigen a good candidate for targeted *immunotherapy*. The goals of our studies are to generate a recombinant PSA adenovirus type 5 (Ad5-PSA) that is safe and effectively activates a PSA-specific T-cell response capable of eliminating *prostate* *cancer* cells, and to characterize the immunologic basis for this rejection. Here we show that immunization of mice with Ad5-*PSA* induced *PSA*-specific cellular and humoral immunity that was protective against a subcutaneous challenge with RM11 *prostate* *cancer* cells expressing *PSA* (RM11psa), but not mock-transfected RM11 tumor cells (RM11neo). Mice immunized with recombinant adenovirus type 5 encoding beta-galactosidase (Ad5-lacZ) did not generate protective immunity. Antitumor activity was predominantly mediated by CD8+ T lymphocytes. Although Ad5-*PSA* immunization prior to RM11psa challenge was protective, Ad5-*PSA* immunization alone was not able to control the growth of existing RM11psa tumors. In contrast, established RM11psa tumors ranging in size from 500 to 1,000 mm3 were efficiently eliminated if Ad5-*PSA* priming was followed 7 days later by intratumoral injection of recombinant canarypox viruses (ALVAC) encoding interleukin-12 (IL-12), IL-2, and tumor necrosis factor...

...but natural killer cells became necessary for a maximal response. These data provide information on the effector cell populations in a protective immune response to *prostate* *cancer* and demonstrate the utility of an Ad5-*PSA* vaccine combined with cytokine gene delivery to eliminate large established tumors that are refractory to other interventional methods.
DESCRIPTORS:
...ORGANISMS: recombinant antigen *vector*; ...

...gene *vector*

4/3,K/9 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12965538 BIOSIS NO.: 200100172687
Retrovirus-mediated gene transfer of prostate specific antigen (*PSA*) into dendritic cell precursors for the *immunotherapy* of *prostate* *cancer*.

AUTHOR: Qin Gangjian(a); [redacted]elley Leslie(a); Peace David(a); [redacted]Medin Jeffrey A (a)
AUTHOR ADDRESS: (a)Department of Medicine, University of Illinois at Chicago, Chicago, IL, 60607**USA
JOURNAL: Cancer Gene Therapy 7 (12):pS27 December, 2000
MEDIUM: print
CONFERENCE/MEETING: Ninth International Conference on Gene Therapy of Cancer San Diego, California, USA December 07-09, 2000
ISSN: 0929-1903
RECORD TYPE: Citation
LANGUAGE: English
SUMMARY LANGUAGE: English

Retrovirus-mediated gene transfer of prostate specific antigen (*PSA*) into dendritic cell precursors for the *immunotherapy* of *prostate* *cancer*.

DESCRIPTORS:
...ORGANISMS: gene *vector*

4/3,K/10 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11512949 BIOSIS NO.: 199800294281
Anti-*PSA* immune responses induced by viral *vector* immunization: A model for *immunotherapy* of *prostate* *cancer*.
AUTHOR: Lubaroff David M; Elzey Bennett D; Ratliff Timothy L
AUTHOR ADDRESS: Iowa City, IA**USA
JOURNAL: Journal of Urology 159 (5 SUPPL.):p9 May, 1998
CONFERENCE/MEETING: 93rd Annual Meeting of the American Urological Association, Inc. San Diego, California, USA May 30-June 4, 1998
SPONSOR: American Urological Association
ISSN: 0022-5347
RECORD TYPE: Citation
LANGUAGE: English

Anti-*PSA* immune responses induced by viral *vector* immunization: A model for *immunotherapy* of *prostate* *cancer*.
MISCELLANEOUS TERMS: ...model, viral *vector* immunization...

4/3,K/11 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11412615 BIOSIS NO.: 199800193947
***Immunotherapy* of *prostate* *cancer*: Anti-*PSA* cytotoxic lymphocytes induced by viral *vector* immunization.**
AUTHOR: Lubaroff D M(a); Elzey B D; Ratliff T L
AUTHOR ADDRESS: (a)Univ. Iowa, Iowa City, IA 52242**USA
JOURNAL: Proceedings of the American Association for Cancer Research Annual Meeting 39p11 March, 1998
CONFERENCE/MEETING: 89th Annual Meeting of the American Association for Cancer Research New Orleans, Louisiana, USA March 28-April 1, 1998
SPONSOR: American Association for Cancer Research
ISSN: 0197-016X
RECORD TYPE: Citation
LANGUAGE: English

***Immunotherapy* of *prostate* *cancer*: Anti-*PSA* cytotoxic lymphocytes induced by viral *vector* immunization.**
...METHODS & EQUIPMENT: viral *vector* immunization...
?ds

Set Items Description

```
S1      14880   (PSA OR [redacted]A OR PAP) (S) (PROSTATE (W) CA[redacted]ER)
S2        197   S1 (S) (IMMUNOTHERAPY OR (IMMUNOGENIC (W) PEPTIDE))
S3         22   S2 AND (PLASMID OR VECTOR)
S4         11   RD (unique items)
?s s2 and (MHC or CTL)
             197  S2
          100738  MHC
           36140  CTL
      S5      38  S2 AND (MHC OR CTL)
?s s5 and (epitope)
              38  S5
           93710  EPITOPE
      S6      20  S5 AND (EPITOPE)
?rd
...completed examining records
      S7       9  RD (unique items)
?s s7 not s4
               9  S7
              11  S4
      S8       8  S7 NOT S4
?t s8/3,k/all
```

8/3,K/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13473796 22120030 PMID: 12124806
Development of HLA-A2402/K(b) transgenic mice.
Gotoh Masashi; Takasu Hideo; Harada Kenji; Yamaoka Takashi
Research Division, Sumitomo Pharmaceuticals, Osaka, Japan.
International journal of cancer. Journal international du cancer (United States) Aug 10 2002, 100 (5) p565-70, ISSN 0020-7136 Journal Code: 0042124
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

HLA-transgenic mice have been developed to facilitate studies of HLA-restricted cytotoxic responses, e.g., for the identification of immunodominant HLA-restricted *CTL* epitopes and the optimization of peptide or DNA vaccine constructs for human use. We have developed HLA-A2402/K(b)-transgenic mice expressing chimeric human...

... domains of H-2K(b)) class I molecules. Immunization of these HLA-A2402/K(b)-transgenic mice with various known HLA-A24-restricted immunodominant cancer *CTL* *epitope* peptides derived from gp100, MAGE-1, MAGE-3, Her2/neu, CEA and TERT induced HLA-A24-restricted, peptide-specific CTLs. Using these transgenic mice, we identified a novel HLA-A24-restricted *CTL* *epitope*, *PSA* (152-160), encoded by human prostate-specific antigen. Staining with HLA tetramers showed that the cytotoxic activity induced by immunizing with *PSA*(152-160) in HLA-A2402/K(b) transgenic mice was HLA-A2402-restricted and CD8-dependent. Therefore, *PSA*(152-160) might be a candidate peptide for vaccination of HLA-A24(+) patients with *prostate* *cancer* . Our results suggest that HLA-A2402/K(b) transgenic mice might be useful in the search for HLA-A24-restricted *CTL* epitopes functioning as human cancer antigens and for the development of peptide-based cancer *immunotherapy*. Copyright 2002 Wiley-Liss, Inc.

8/3,K/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13445833 22065164 PMID: 12070713
Induction of Tc2 cells with specificity for prostate-specific antigen from patients with hormone-refractory prostate cancer.
Perambakam Supriya; Xue Bao-Hua; Sosman Jeffrey A; Peace David J

Section of Hematology/Oncology (M/C 734), Room 3150, Molecular Biology Research Building, 900 S. Ashland Avenue, The University of Illinois at Chicago, Chicago, IL 60607, USA.
Cancer immunology, immunotherapy : CII (Germany) Jul 2002, 51 (5) p263-70, ISSN 0340-7004 Journal Code: 8605732
Contract/Grant No.: R21 CA88062; CA; NCI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Prostate-specific antigen (PSA) is a potentially useful antigen for targeted T-cell *immunotherapy* of *prostate* *cancer* (CaP). Our laboratory has identified a synthetic nonamer peptide (*PSA* 146-154) homologue of *PSA*, which binds to the prevalent human leukocyte antigen, HLA-A2, and elicits specific cytotoxic T-lymphocyte (*CTL*) responses from normal individuals of the HLA-A2 phenotype. In the present study, we report on the induction of *CTL* from peripheral blood mononuclear cells (PBMC) of patients with hormone-refractory CaP, which exhibit the same specificity. T-cell lines were established from two patients by stimulation of PBMC with *PSA* 146-154 peptide in vitro. The T-cell lines exhibited specific cytolytic activity against T2 cells pulsed with *PSA* 146-154 peptide, but not a control HLA-A2 binding peptide (HIV-RT 476-484) via chromium release assay (CRA). The T-cell lines also showed *PSA* 146-154 peptide-specific IL-4 responses, but no detectable interferon-gamma (IFN-gamma) responses via enzyme-linked immuno-spot assays. Magnetic immuno-selection studies...

... 4) responses were mediated by CD8(+), but not by CD4(+) T cells. This Tc2 line was further characterized for the ability to recognize endogenously processed *PSA* epitopes. The line specifically secreted IL-4 in response to HLA-A2(+) target cells transfected to express *PSA* and specifically lysed the *PSA*(+) target cells, but not control transfected cells. The results indicate that the *PSA* 146-154 peptide emulates a naturally processed and presented peptide *epitope* of *PSA* that is within the T-cell repertoire of HLA-A2(+)patients with CaP.

8/3,K/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09975307 98414319 PMID: 9743387

Generation of human cytolytic T lymphocyte lines directed against prostate-specific antigen (PSA) employing a PSA oligoepitope peptide.

Correale P; Walmsley K; Zaremba S; Zhu M; Schlom J; Tsang K Y
Laboratory of Tumor Immunology and Biology, Division of Basic Science, National Cancer Institute, Bethesda, MD 20892, USA.
Journal of immunology (Baltimore, Md. : 1950) (UNITED STATES) Sep 15 1998, 161 (6) p3186-94, ISSN 0022-1767 Journal Code: 2985117R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Prostate-specific Ag (*PSA*), which is expressed in a majority of prostate cancers, is a potential target for specific *immunotherapy*. Previous studies have shown that two 10-mer *PSA* peptides (designated *PSA*-1 and *PSA*-3) selected to conform to human HLA class I-A2 motifs can elicit *CTL* responses in vitro. A longer *PSA* peptide (30-mer) designated *PSA*-OP (oligoepitope peptide), which contains both the *PSA*-1 and *PSA*-3 HLA-A2 epitopes and an additional potential *CTL* *epitope* (designated *PSA*-9) for the HLA-class I-A3 allele, was investigated for the ability to induce cytotoxic T cell activity. T cell lines from different HLA-A2 and HLA-A3 donors were established by in vitro stimulation with *PSA*-OP; the *CTL* lines lysed *PSA*-OP as well as *PSA*-1- or *PSA*-3-pulsed C1R-A2 cells, and *PSA*-OP and *PSA*-9-pulsed C1R-A3 cells, respectively. The *CTL* lines derived from the *PSA*-OP peptide also lysed *PSA*-positive

prostate *cancer* cells. *PSA* -OP-derived T cell lines also lysed recombinant vaccinia-*PSA* -infected targets but not targets infected with wild-type vaccinia. *PSA*-OP did not bind HLA-A2 and HLA-A3 molecules. The decrease in cytotoxicity in the presence of protease inhibitors suggests that the *PSA* -OP is cleaved into shorter peptides, which in turn can interact with HLA-class I molecules and, as a consequence, induce *CTL* -mediated lysis. We have also demonstrated that it is possible to induce *CTL* responses in HLA-A2.1/Kb transgenic mice by immunization with *PSA* -OP with adjuvant. These studies thus provide evidence that oligopeptides such as *PSA* -OP may be useful candidates for peptide-based cancer vaccines.

8/3,K/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09294087 97203572 PMID: 9051144
Induction of human cytotoxic T lymphocytes specific for prostate-specific antigen.
Xue B H; Zhang Y; Sosman J A; Peace D J
Department of Medicine, Loyola University Medical Center, Maywood, Illinois 60153, USA.
Prostate (UNITED STATES) Feb 1 1997, 30 (2) p73-8, ISSN 0270-4137 Journal Code: 8101368
Comment in Prostate. 1997 Jun 15;32(1) 73-4; Comment in PMID 9207960
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Prostate-specific antigen (*PSA*), a tissue-specific protein expressed by most adenocarcinomas of the prostate, might be a useful target for T-cell-mediated *immunotherapy* of prostate cancers. The current study examined whether it is possible to elicit human cytotoxic T lymphocytes (*CTL*) with specificity for *PSA* . A synthetic nonamer peptide, corresponding to residues 146-154 of *PSA* and containing a canonical HLA-A2-binding motif, was shown to stabilize the expression of HLA-A2 on the T2 antigen-processing mutant cell line. Repeated in vitro stimulation of peripheral blood lymphocytes from a normal HLA-A2+ donor induced *CTL* with specificity for the *PSA* 146-154 peptide. The peptide-induced *CTL* expressed the CD4- CD8+ cell surface phenotype and were restricted by HLA-A2. A large portion of patients with *prostate* *cancer* express the HLA-A2 phenotype, implying that many prostate cancers might be targeted by HLA-A2-restricted *CTL* with specificity for the *PSA* 146-154 *epitope*.

8/3,K/5 (Item 1 from file: 159)
DIALOG(R)File 159:Cancerlit
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02415744 PMID: 98641144
In vitro generation of prostate specific antigen (PSA) specific cytotoxic T-cell lines using recombinant vaccinia-PSA infected dendritic cells (Meeting abstract).
Correale; Tsang; Zhu; Zaremba; Walmsley; Lora; Schlom
Laboratory of Tumor Immunology and Biology, NCI, NIH, Bethesda, MD 20892
Proc Annu Meet Am Assoc Cancer Res 1997, 38, ISSN 0197-016X
Document Type: MEETING ABSTRACTS
Languages: ENGLISH
Main Citation Owner: NOTNLM
Record type: Completed

Prostate specific antigen (*PSA*) is a serine protease and member of the kallilrein gene family. *PSA*, expressed in a majority of prostate cancers, is a potential target for specific *immunotherapy*. Previous studies have shown that 3 peptides [*PSA*-1: FLPTKKLQCV; *PSA*-3: VISNDVCAQV; and *PSA*

-oligo-*epitope* peptide *PSA*-OP): FLTPKKLQCVDLHVIS NDV Q VHPQKVTK], can elicit *CTL* responses in both normal donors and patients with *prostate* *cancer*. The ability of dendritic cells (DCs) infected with rV-*PSA* (recombinant *PSA*-vaccinia construct) or rV-*PSA*-OP (recombinant *PSA* -OP-vaccinia construct), to promote the in vitro generation of autologous *PSA* specific CTLs was investigated. Dendritic cells were expanded from peripheral blood mononuclear cells (PBMC) by culturing in vitro for 5-7 days in medium containing...

... to 7 IVS when autologous PBMCs were used as antigen presenting cells). The specificity of these T cell lines were determined by cytotoxic assays using *PSA* peptide pulsed C1R-A2 cells, C1R-A2 cells infected with rV- *PSA* or rV-*PSA*-OP as well as LNCaP cells. They lysed *PSA*-1, *PSA*-3 or *PSA*-OP pulsed C1R-A2 cells, and *PSA* positive, HLA-A2 positive *prostate* *cancer* cells. These CTLs also lysed rV-*PSA* and rV-*PSA*-OP infected target cells. The specificity of the lysis was defined by the inability of the *CTL* to Aso *PSA* negative carcinoma targets, the blocking of Easiest with anti-HLA-A2 antibody and the inability of the cold K562 target to inhibit lysis. These findings demonstrate for the first time (a) the ability to generate *CTL* response to defined *PSA* epitopes using rV-*PSA* and rV-*PSA* -OP infected DCs; (b) the ability of LNCaP cells to endogenously precess *PSA* to present peptide in the context of major histocompatibility complex (*MHC*) for *CTL* lysis; and (c) the ability of DCs to endogenously process rV-*PSA* and rV-*PSA*-OP to present specific *PSA* peptides in the context of *MHC* for T cell mediated lysis.

8/3,K/6 (Item 2 from file: 159)
DIALOG(R)File 159:Cancerlit

02321884 PMID: 97600636

Generation of human t-cell lines specific for prostate specific antigen using an oligo-*epitope* profile (Meeting abstract).

Correale; Tasang; Walmsley; Nieroda; Zaremba; Schlom
Lab. of Tumor Immunology and Biology, NCI, NIH, Bethesda, MD, 20892

Proc Annu Meet Am Assoc Cancer Res 1996, 37, ISSN 0197-016X
Document Type: MEETING ABSTRACTS
Languages: ENGLISH
Main Citation Owner: NOTNLM
Record type: Completed

Generation of human t-cell lines specific for prostate specific antigen using an oligo-*epitope* profile (Meeting abstract).

Prostate specific antigen (*PSA*), which is expressed in a majority of prostate cancers, is a potential target for specific *immunotherapy*. Previous studies have shown that 2 *PSA* peptides (*PSA*-1 and *PSA*-3), 10-mers, selected to conform to human HLA class 1-A2 motifs, can elicit *CTL* responses in both normal donors and patients with *prostate* *cancer* . A longer *PSA* peptide (30-mer), designated *PSA*-OP (oligo-*epitope* peptide), containing the shorter *PSA*-1 and *PSA*-3 peptide sequences, was investigated for the ability to mediate cytotoxic T-cell activity. Two T-cell lines from different normal donors were established by in vitro stimulation with *PSA*-OP. Specificity of these lines for the stimulating peptide was determined by cytotoxicity assays using peptide pulsed CIR-A2 cells. The *CTL* were phenotypically CD4+ CD8+, or CD4+/CD8+ and CD56-. They lysed *PSA*-OP as well as *PSA*-1- or *PSA*-3-pulsed CIR-A2 cells, and *PSA*-positive *prostate* *cancer* cells. These T-cell lines also lysed rV- *PSA* (recombinant *PSA*-vaccinia construct) infected targets. *PSA*-OP did not bind HLA-A2 molecules as indicated by the lack of upregulation of A2 expression on 174CEM-T2 cells. The decrease in cytotoxicity in the presence of protease inhibitors suggested that the *PSA*-OP must be cleaved into shorter peptides which in turn can interact with HLA-A2 molecules and, as a consequence, induce *CTL* lysis of CIR-A2 cells. Recognition by *CTL* suggests that *PSA* -OP peptide may be a potential candidate for use in peptide-based vaccines.

8/3,K/7 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13725076 BIOSIS NO.: 200200353897
Induction of Tc2 cells with specificity for prostate specific antigen from patients with advanced stage prostate cancer.
AUTHOR: Perambakam Supriya M(a); Xue Bao-Hue(a); Sosman Jeffrey A(a); Peace David J(a)
AUTHOR ADDRESS: (a)Medicine, University of Illinois, 900 S Ashland Avenue, Chicago, IL, 60607**USA
JOURNAL: FASEB Journal 16 (4):pA336 March 20, 2002
MEDIUM: print
CONFERENCE/MEETING: Annual Meeting of the Professional Research Scientists on Experimental Biology New Orleans, Louisiana, USA April 20-24, 2002
ISSN: 0892-6638
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: *Prostate* *cancer* (Pca) cells express tissue-specific proteins that are potential targets for directed *immunotherapy*. We previously identified a peptide homologue of prostate specific antigen (*PSA* 146-154), which binds to HLA-A2 and elicits specific cytotoxic T lymphocyte (*CTL*) responses from normal individuals. Here we report the induction and characterization of *CTL* with the same specificity from patients with advanced Pca. T-cell lines were induced from peripheral blood mononuclear cells of two patients with stage D3a...

...in-vitro stimulation with peptide. T-cell lines elicited from both patients showed peptide-specific IL-4 responses and cytotoxicity against T2 cells pulsed with *PSA* 146-154 peptide and HLA-A2+ target cells transfected to express *PSA*. Immuno-selection studies demonstrated that both cytotoxic and IL-4 responses were mediated by CD8+, but not CD4+, T cells. This is the first report of the induction of *PSA* peptide-specific *CTL* of the Tc2 phenotype from patients with advanced Pca. The results demonstrate that the T cell repertoire of Pea patients contains inducible *CTL* with specificity for a peptide that corresponds to a naturally processed *epitope* of *PSA*.

8/3,K/8 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

11806618 EMBASE No: 2002376370
Recognition of prostate tumor cells by cytotoxic T lymphocytes specific for prostate-specific membrane antigen
Lu J.; Celis E.
E. Celis, Department of Immunology, Mayo Clinic, Rochester, MN 55905 United States
AUTHOR EMAIL: celis.esteban@mayo.edu
Cancer Research (CANCER RES.) (United States) 15 OCT 2002, 62/20 (5807-5812)
CODEN: CNREA ISSN: 0008-5472
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 31

The development of *immunotherapy* for cancer, such as synthetic peptide-based vaccines, relies heavily on the identification of appropriate epitopes capable of eliciting antitumor T-cell responses. We have...

...of computer-based algorithms to predict peptide sequences from prostate-specific membrane antigen (PSMA) capable of stimulating in vitro

CTLs restricted by the H[redacted]-A2 *MHC* molecule. Four of the[redacted]ive peptides that were predicted by these algorithms were capable of inducing antigen-specific CTLs that killed target cells that were...

...PSMA molecules. These results underline the importance of demonstrating antitumor reactivity of peptide-induced CTLs for the selection of epitopes destined to become immunotherapeutic for *prostate* *cancer*.
DRUG DESCRIPTORS:
HLA A2 antigen--endogenous compound--ec; *epitope*--endogenous compound--ec ; synthetic peptide; cancer vaccine
?ds

Set	Items	Description
S1	14880	(PSA OR PSMA OR PAP) (S) (PROSTATE (W) CANCER)
S2	197	S1 (S) (IMMUNOTHERAPY OR (IMMUNOGENIC (W) PEPTIDE))
S3	22	S2 AND (PLASMID OR VECTOR)
S4	11	RD (unique items)
S5	38	S2 AND (MHC OR CTL)
S6	20	S5 AND (EPITOPE)
S7	9	RD (unique items)
S8	8	S7 NOT S4

?rd s5
...completed examining records
S9 19 RD S5 (unique items)
?s s9 not s7
19 S9
9 S7
S10 11 S9 NOT S7
?t s10/3,k/all

10/3,K/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13731733 22272611 PMID: 12384542
Recognition of Prostate Tumor Cells by Cytotoxic T Lymphocytes Specific for Prostate-specific Membrane Antigen.
Lu Jun; Celis Esteban
Department of Immunology, Mayo Graduate School, and Mayo Cancer Center, Mayo Clinic, Rochester, Minnesota 55905.
Cancer research (United States) Oct 15 2002, 62 (20) p5807-12, ISSN 0008-5472 Journal Code: 2984705R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: In Process

The development of *immunotherapy* for cancer, such as synthetic peptide-based vaccines, relies heavily on the identification of appropriate epitopes capable of eliciting antitumor T-cell responses. We have used a combination of computer-based algorithms to predict peptide sequences from prostate-specific membrane antigen (*PSMA*) capable of stimulating in vitro CTLs restricted by the HLA-A2 *MHC* molecule. Four of the five peptides that were predicted by these algorithms were capable of inducing antigen-specific CTLs that killed target cells that were pulsed exogenously with the corresponding peptides. However, only one of the four peptides, *PSMA* (27), induced CTLs that were effective at recognizing prostate tumor cells expressing the HLA-A2 and *PSMA* molecules. These results underline the importance of demonstrating antitumor reactivity of peptide-induced CTLs for the selection of epitopes destined to become immunotherapeutic for *prostate* *cancer*.

10/3,K/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09882618 98317971 PMID: 9655265

Induction of prostat[redacted] tumor-specific CD8+ cytotoxi[redacted]-lymphocytes in vitro using antigen-presenting cells pulsed with prostatic acid phosphatase peptide.

Peshwa M V; Shi J D; Ruegg C; Laus R; van Schooten W C
Dendreon Corporation, Mountain View, California 94043, USA. mvpeshwa@dendreon.com

Prostate (UNITED STATES) Jul 1 1998, 36 (2) p129-38, ISSN 0270-4137 Journal Code: 8101368
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

BACKGROUND: Most strategies in cancer *immunotherapy* are aimed at the induction of a strong cellular immune response against the tumor. Particularly, CD8+ T lymphocytes have been proven in multiple animal models ...

... peripheral blood-derived antigen-presenting cells (APC), containing dendritic cells (DC), to generate prostate tumor-specific CD8+ T cells. Selected peptides from prostatic acid phosphatase (*PAP*), a prostate tissue-specific antigen, were shown to bind HLA-A2. A high-affinity peptide was used to generate peptide-specific CD8+ cytolytic T lymphocytes (*CTL*) from the peripheral blood of healthy donors. RESULTS: The obtained *PAP* -peptide-specific *CTL* lysed peptide-coated target cells, vaccinia-infected target cells, and HLA-A2-positive prostate-tumor cells in vitro in an antigen-specific manner. CONCLUSIONS: Our results indicate that *CTL* precursors to the *PAP* gene product exist and could be potentially recruited to elicit an antitumor response. Thus, *PAP* is a suitable antigen for inclusion in *prostate* *cancer* vaccines.

10/3,K/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09793112 98227629 PMID: 9568678

Report of immune monitoring of prostate cancer patients undergoing T-cell therapy using dendritic cells pulsed with HLA-A2-specific peptides from prostate-specific membrane antigen (PSMA).

Salgaller M L; Lodge P A; McLean J G; Tjoa B A; Loftus D J; Ragde H; Kenny G M; Rogers M; Boynton A L; Murphy G P
Northwest Biotherapeutics, L.L.C., Pacific Northwest Cancer Foundation, Seattle, Washington 98125, USA. mls@nwbio.org

Prostate (UNITED STATES) May 1998, 35 (2) p144-51, ISSN 0270-4137 Journal Code: 8101368
Document type: Clinical Trial; Clinical Trial, Phase II; Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

... test and enzyme-linked immunosorbant assay (ELISA). CONCLUSIONS: Our initial observations using an ELISA and DTH test indicate that we are enhancing cellular immunity in *prostate* *cancer* patients following infusion with DC plus *PSMA*-derived peptides. Several methods are underway to comprehensively monitor both cell-mediated and humoral immune responsiveness, including: determining anti-*PSMA* serum antibody titers, testing immunogen-restricted responder-cell proliferation and cytotoxicity, assessing aberrations in signal transduction, antigen processing, and presentation, and measuring soluble factors that...
; Enzyme-Linked Immunosorbent Assay; Genes, *MHC* Class I; Treatment Outcome

10/3,K/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09572094 97461426 PMID: 9317107

Induction of tissue-specific autoimmune prostatitis with prostatic acid phosphatase immunization: implications for immunotherapy of prostate cancer.

Fong L; Ruegg C L; Brockstedt D; Engleman E G; Laus R
Stanford University School of Medicine, CA 94305, USA.

Journal of immunology (Baltimore, Md. : 1950) (UNITED STATES) Oct 1 1997, 159 (7) p3113-7, ISSN 0022-1767 Journal Code: 2985117R
Contract/Grant No.: CA71725; CA; NCI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Prostatic acid phosphatase (PAP) is uniquely expressed in prostatic tissue and prostate cancer. In this study, the immunogenicity of *PAP* was investigated in a male rat model. We show that immunization with recombinant rat or human *PAP* in CFA leads to a significant Ab response, but does not generate *CTL* or result in autoimmune prostatitis. In contrast, immunization with recombinant vaccinia expressing human *PAP*, but not rat *PAP*, generates a *CTL* response and tissue-specific prostatitis in the absence of detectable *PAP*-specific Abs. These findings suggest that a cellular immune response to *PAP*, rather than Abs, mediates destructive autoimmune prostatitis. Thus, xenogeneic forms of *PAP* are a new tool for the induction of prostate-specific immunity and may prove useful for the *immunotherapy* of *prostate* *cancer*.

10/3,K/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09048089 96427376 PMID: 8830740

Expression of human prostate-specific antigen (PSA) in a mouse tumor cell line reduces tumorigenicity and elicits PSA-specific cytotoxic T lymphocytes.

Wei C; Storozynsky E; McAdam A J; Yeh K Y; Tilton B R; Willis R A; Barth R K; Looney R J; Lord E M; Frelinger J G
Cancer Center Immunology Unit, University of Rochester, NY 14642, USA.

Cancer immunology, immunotherapy : CII (GERMANY) Jul 1996, 42 (6) p362-8, ISSN 0340-7004 Journal Code: 8605732
Contract/Grant No.: CA70218; CA; NCI; POAG104643A; OA; SAMHSA; T32CA09363 ; CA; NCI; +
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Human prostate-specific antigen (*PSA*) has a highly restricted tissue distribution. Its expression is essentially limited to the epithelial cells of the prostate gland. Moreover, it continues to be synthesized by prostate carcinoma cells. This makes *PSA* an attractive candidate for use as a target antigen in the *immunotherapy* of *prostate* *cancer*. As a first step in characterizing the specific immune response to *PSA* and its potential use as a tumor-rejection antigen, we have incorporated *PSA* into a well-established mouse tumor model. Line 1, a mouse lung carcinoma, and P815, a mouse mastocytoma, have been transfected with the cDNA for human *PSA*. Immunization with a *PSA*-expressing tumor cell line demonstrated a memory response to *PSA* which protected against subsequent challenge with *PSA*-expressing, but not wild-type, tumors. Tumor-infiltrating lymphocytes could be isolated from *PSA*-expressing tumors grown in naive hosts and were specifically cytotoxic against a syngeneic cell line that expressed *PSA* . Immunization with tumor cells resulted in the generation of primary and memory cytotoxic T lymphocytes (*CTL*) specific for *PSA* . The isolation of *PSA*-specific *CTL* clones from immunized animals further demonstrated that *PSA* can serve as a target antigen for antitumor *CTL*. The immunogenicity studies carried out in this mouse tumor model provide a

rationale for the design of methods to elicit *PSA*-specific cell-mediated immunity in humans.

10/3,K/6 (Item 1 from file: 159)
DIALOG(R)File 159:Cancerlit

02413990 PMID: 98639386
Immunogenicity of prostatic acid phosphatase in the Copenhagen rat (Meeting abstract).
Fong; Brockstedt; Laus; Ruegg; Engleman
Stanford University School of Medicine, Stanford, CA 94305
Proc Annu Meet Am Assoc Cancer Res 1997, 38, ISSN 0197-016X
Document Type: MEETING ABSTRACTS
Languages: ENGLISH
Main Citation Owner: NOTNLM
Record type: Completed

Prostatic tissues and *prostate* *cancer* express several tissue specific antigens including prostatic acid phosphatase (*PAP*) and prostate specific antigen. Of these, *PAP* shares the least homology to other non-specific proteins. The ability of *PAP* to serve as an immunogen and as a potential target for *immunotherapy* was explored in the Dunning rat prostate tumor model. Male Copenhagen rats were immunized with *PAP* in Freunds adjuvant, antigen pulsed dendritic cells (DC), and vaccinia constructs containing *PAP*. *PAP* -specific antibody responses were detected in those animals immunized with *PAP* in Freunds adjuvant. Although no lymphocyte proliferative responses could be detected to rat *PAP* in any of the animals, proliferation to human *PAP* was demonstrated in immunized rats. *PAP*-specific *CTL* activity was detected in animals receiving antigen pulsed dendritic cells and vaccinia constructs. Finally, inflammation within the prostate gland was seen in rats immunized with the recombinant *PAP* vaccinia construct. These preliminary studies suggest that tolerance to self-antigens can be broken, and that tissue specific antigens may be targeted for *immunotherapy*. Future experiments will focus on optimization of *PAP* immunogenicity, tumor protection, and tumor treatment studies in this animal system. The results of these experiments will form the basis of a Phase I human trial immunizing patients with hormone refractory *prostate* *cancer* with antigen pulsed DC.

10/3,K/7 (Item 2 from file: 159)
DIALOG(R)File 159:Cancerlit

02319267 PMID: 96649903
Targeted *CTL* -mediated immunity for prostate cancer: development of human PSA-expressing transgenic mice (Meeting abstract).
Erelinger; Wei; Willis; Storozynsky; Tilton; Barth; Lord
Cancer Center and Dept. of Microbiology and Immunology, Univ. of Rochester Medical Center, Rochester, NY 14642
Proc Annu Meet Am Assoc Cancer Res 1996, 37, ISSN 0197-016X
Document Type: MEETING ABSTRACTS
Languages: ENGLISH
Main Citation Owner: NOTNLM
Record type: Completed

Targeted *CTL* -mediated immunity for prostate cancer: development of human PSA-expressing transgenic mice (Meeting abstract).
...antigen (PSA) in the epithelial cells of the prostate gland makes it a potential candidate for use as a target antigen in the immunotherapy of *prostate* *cancer* . Using the mouse tumors P815 and line 1 each transfected with human *PSA*, we have shown that mice generate a vigorous specific cytotoxic T lymphocyte (*CTL*) response to this antigen. Further, mice immunized with P815/*PSA* are protected against a subsequent challenge

with line1/*PSA* tumor cells. We have developed transgenic mice carrying the human *PSA* gene and its regulatory elements in order to express human *PSA* in the prostate of mice. We have identified by Southern blot analysis, 23 lines of mice which have incorporated differing numbers of the *PSA* transgene. *PSA* is present in the serum of the mice at varying levels. Further analysis of the tissue distribution of *PSA* using PCR is underway and will be presented. This transgenic mouse model will allow us to develop methods for generating an autoimmune, cell-mediated response against *PSA* which will be translatable to the *immunotherapy* of human *prostate* *cancer*.

10/3,K/8 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13814821 BIOSIS NO.: 200200443642
Transgenic mice co-expressing *PSA* and human HLA: A 'humanized' transgenic model for *prostate* *cancer* *immunotherapy* development.
AUTHOR: Hollenbeck Brent K(a); Priyadarsiny Priyanka(a); DeFeo-Jones Deborah; Neeley Cindy(a); Vessella Robert; June Escara-Wilke(a); Hwang Clara(a); Rubin Mark(a); Sanda Martin G(a)
AUTHOR ADDRESS: (a)Ann Arbor, MI**USA
JOURNAL: Journal of Urology 167 (4 Supplement):p51 April, 2002
MEDIUM: print
CONFERENCE/MEETING: Annual Meeting of the American Urology Association, Inc. Orlando, Florida, USA May 25-30, 2002
ISSN: 0022-5347
RECORD TYPE: Citation
LANGUAGE: English

Transgenic mice co-expressing *PSA* and human HLA: A 'humanized' transgenic model for *prostate* *cancer* *immunotherapy* development.
DESCRIPTORS:
CHEMICALS & BIOCHEMICALS: ...class I *MHC* {class I major histocompatibility complex...

10/3,K/9 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13765851 BIOSIS NO.: 200200394672
***PSA* transgenic mice co-expressing humanized class I *MHC* as a refined model for *prostate* *cancer* *immunotherapy* development.**
AUTHOR: Priyadarsiny Priyanka(a); Hollenback Brent K; Escara-Wilke June F; DeFeo-Jones Deborah; Vessella Robert; Neeley Yilin C; Hwang Clara; Rubin Mark A; Sanda Martin G
AUTHOR ADDRESS: (a)University of Michigan, Ann Arbor, MI**USA
JOURNAL: Proceedings of the American Association for Cancer Research Annual Meeting 43p278 March, 2002
MEDIUM: print
CONFERENCE/MEETING: 93rd Annual Meeting of the American Association for Cancer Research San Francisco, California, USA April 06-10, 2002
ISSN: 0197-016X
RECORD TYPE: Citation
LANGUAGE: English

***PSA* transgenic mice co-expressing humanized class I *MHC* as a refined model for *prostate* *cancer* *immunotherapy* development.**
DESCRIPTORS:
CHEMICALS & BIOCHEMICALS: ...class I *MHC* {class I major histocompatibility complex...

10/3,K/10 (Item 3 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

13612570 BIOSIS NO.: 200200241391
Vaccination of cancer patients against telomerase: A phase I study using peptide-pulsed dendritic cells.
AUTHOR: Vonderheide Robert H(a); Domchek Susan M(a); Hahn William C(a); George Daniel J(a); Stephans Katherine F(a); Schultze Joachim L(a); Nadler Lee M(a)
AUTHOR ADDRESS: (a)Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA**USA
JOURNAL: Blood 98 (11 Part 1):p508a November 16, 2001
MEDIUM: print
CONFERENCE/MEETING: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Immunological profiling of the telomerase reverse transcriptase (TERT) suggests the potential ability of this enzyme to serve as a target for widely applicable *immunotherapy* against cancer. Data from human and murine systems demonstrate that cytotoxic T lymphocytes can recognize TERT-derived peptides and lyse TERT-positive tumors of multiple...
...initial results of the first clinical trial to vaccinate cancer patients (pts) therapeutically against TERT peptide. 7 HLA-A2 pts with advanced cancer (5 with *prostate* *cancer*, 2 with breast cancer) were vaccinated up to six times subcutaneously every other week with autologous monocyte-derived immature dendritic cells (DC) pulsed ex vivo...

...transient fatigue) and no higher grade toxicity. Bone marrow toxicity was not observed. Among 4 evaluable pts who have completed six vaccines, serum tumor markers (*PSA* or CA 27-29) decreased transiently and modestly in 3 pts. Two of these pts had radiographically stable disease (both 4+ months) and two had...

...3 of 5 patients tested (stimulation indices 7.8 to 95.0, with baseline stimulation indices and indices of normal donor cells <2.0). Peptide/ *MHC* tetramer analysis of fresh peripheral blood indicated a low-level CD8+ post-vaccination reactivity to I540 peptide in 4 of 4 pts tested (0.12...

10/3,K/11 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

11597844 EMBASE No: 2002170775
Immunotherapy for advanced hormone refractory prostate cancer with cytotoxic T lymphocyte precursor-oriented peptide vaccine
Noguchi M.; Hirabayashi Y.; Noda S.; Yamana H.; Suetsugu N.; Itoh K.
M. Noguchi, Department of Urology, Kurume University School of Medicine, Kurume Japan
Nishinihon Journal of Urology (NISHINIHON J. UROL.) (Japan) 2002, 64/4 (253-259)
CODEN: NHJUA ISSN: 0029-0726
DOCUMENT TYPE: Journal ; Conference Paper
LANGUAGE: JAPANESE SUMMARY LANGUAGE: ENGLISH; JAPANESE
NUMBER OF REFERENCES: 19

There is a lack of effective therapeutic regimens for advanced hormone-refractory *prostate* *cancer* (HRPC). Recent combination regimens of chemotherapy have improved the management of HRPC. Neither systemic chemotherapy nor radiation regimens have significantly improved survival. New approaches with cancer peptides recognized by T-cells in *immunotherapy* for *prostate* *cancer* have been investigated. A phase I